Rearrangements and Transalkylation of *t*-Butylthiophenes

HANS WYNBERG AND U. E. WIERSUM[1]

Department of Organic Chemistry, The University, Bloemsingel 10, Groningen, The Netherlands

Received November 16, 1964

2,4- and 2,5-di-*t*-butylthiophene were prepared by alkylation of thiophene and separation by chloromercuration. Isomerization of 2- and 3-*t*-butylthiophene in the presence of aluminum chloride gives polymeric products plus traces of dialkyl products; 2,5-di-*t*-butylthiophene is converted to the 2,4-isomer. Transalkylation of 2,5-dimethylthiophene by 2,5-di-*t*-butylthiophene gave the 3-*t*-butyl-2,5-dimethyl product.

Although the alkylation, rearrangement, and transalkylation of alkylbenzenes under the influence of Friedel–Crafts catalysts has been the subject of intensive study,[2,3] our knowledge of the behavior of alkylthiophenes is limited.

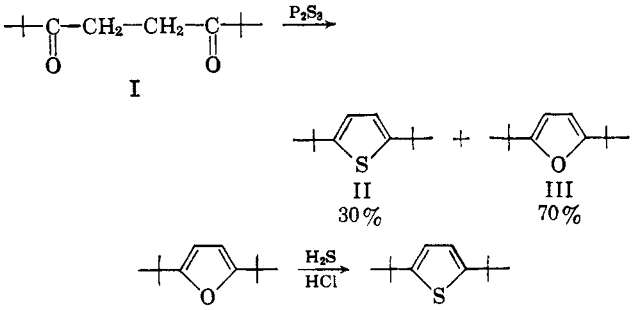
Hartough, Ceasar, and co-workers[4] carried out fundamental studies on the alkylation of thiophene more than 15 years ago and more recently Russian chemists[5] have made notable contributions. Nevertheless, no clear-cut example of the isomerization of an alkylthiophene nor of a transalkylation (disproportionation) appears to have been reported.[5]

This paper reports evidence on the rearrangement as well as transalkylation behavior of several *t*-butylthiophenes under the influence of aluminum chloride.

Preparation of Starting Materials.—Initial studies in our laboratory had shown that a minimum number of side reactions, particularly polymerization, would be encountered if the isomeric *t*-butylthiophenes were used. To this end we prepared pure samples of 2- and 3-*t*-butylthiophene and of 2,5- and 2,4-di-*t*-butylthiophene. Although the monosubstituted isomers have been prepared previously,[6-11] the preparation of the pure disubstituted thiophenes needed considerable improvement.[8,10] No *o*-di-*t*-butylthiophenes are known. Attempts in this laboratory[12,13] to prepare 3,4-di-*t*-butylthiophene *via* 2,3-di-*t*-butylbutadiene have failed thus far. Weinmayer's claim[14] to have prepared 2,3,4,5-tetra-*t*-butylthiophene could not be substantiated.[15]

2-*t*-Butylthiophene, b.p. 163° (751 mm.), prepared according to Sy's[9] directions, was identical with that reported[8,11] and its purity by v.p.c. was above 99%. The 3-*t*-butylthiophene[8] could be isolated in gram quantities by preparative v.p.c. of the residue remaining after distillation of the 2-isomer.

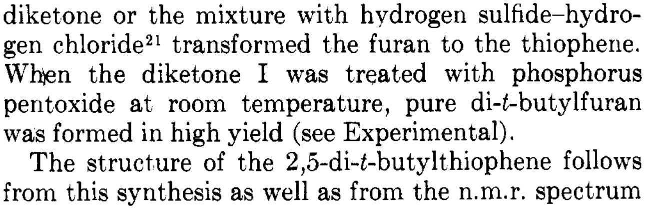
Using excess *t*-butyl chloride in the alkylation of thiophene a 43% yield of dialkylated products, b.p. 221–222° (752 mm.), was obtained. The 2,5- and 2,4-isomers were present in the ratio 3:1 as shown by v.p.c. The largest peak corresponded to 2,5-di-*t*-butylthiophene as shown by an independent synthesis of this material from 2,2,7,7-tetramethyloctane-3,6-dione (I). The 2,5-di-*t*-butylthiophene obtained in this manner had b.p. 222° (751 mm.), m.p. 22–23°. The synthesis *via* the diketone deserves some comment.



When the diketone I[16-19] was treated with phosphorus trisulfide, 2,5-di-*t*-butylfuran (III)[19,20] and 2,5-di-*t*-butylthiophene (II) were formed. Separation by distillation was possible. However treatment of the diketone or the mixture with hydrogen sulfide–hydrogen chloride[21] transformed the furan to the thiophene. When the diketone I was treated with phosphorus pentoxide at room temperature, pure di-*t*-butylfuran was formed in high yield (see Experimental).

The structure of the 2,5-di-*t*-butylthiophene follows from this synthesis as well as from the n.m.r. spectrum which shows one sharp singlet at τ 8.67 and one at 3.54 (area ratio 9:1).

The 2,4-di-*t*-butylthiophene was isolated as follows. Treatment of the dialkylated mixture with mercuric chloride furnished one pure mercuri salt, m.p. 117–118°. Its structure (IV) is supported by elementary



---

[1] Predoctoral Fellow of the Netherlands Organization for Pure Scientific Research (Z.W.O.).

[2] For recent literature, see S. H. Patinkin and B. S. Freidman in "Friedel Crafts and Related Reactions," Vol. II, G. Olah, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p. 105.

[3] G. Olah, M. W. Meyer, and N. A. Overchuk, *J. Org. Chem.*, **29**, 2310 (1964).

[4] For a summary, see H. D. Hartough, "Thiophene and its Derivatives," Interscience Publishers, Inc., New York, N. Y., 1952, p. 159.

[5] S. Gronowitz in "Advances in Heterocyclic Chemistry," A. Katritzky, Ed., Academic Press Inc., New York, N. Y., 1964, p. 1.

[6] M. Kutz and B. B. Corson, *J. Am. Chem. Soc.*, **68**, 1477 (1946).

[7] P. D. Ceasar, *ibid.*, **70**, 3623 (1948).

[8] W. G. Appleby, A. F. Sartor, S. H. Lee, and S. W. Kapranos, *ibid.*, **70**, 1552 (1948).

[9] M. Sy, Ng. Ph. Buu Hoi, and Ng. D. Xuong, *J. Chem. Soc.*, 1975 (1954).

[10] Ya. L. Goldfarb and I. S. Korsakova, *Dokl. Akad. Nauk SSSR*, **89**, 301 (1953); *Chem. Abstr.*, **48**, 7598*b* (1954).

[11] P. Cagniant and P. Cagniant, *Bull. soc. chim. France*, 1152 (1956).

[12] H. J. Backer, *Rec. trav. chim.*, **58**, 643 (1939).

[13] H. Wynberg, Ae. de Groot, and D. W. Davies, *Tetrahedron Letters*, 1083 (1963).

[14] V. Weinmayer, *J. Am. Chem. Soc.*, **72**, 918 (1950).

[15] *Cf.* ref. 2, p. 108. Friedman's rationalization seems valid, however; see H. Wynberg and U. E. Wiersum, *Chem. Commun.*, 1 (1965).

[16] M. S. Kharash, H. C. McBay, and W. H. Urry, *J. Am. Chem. Soc.*, **70**, 1275 (1948).

[17] A. Petrov, E. Sokolova, and C. Lan Gao, *Bull. soc. chim. France*, 178 (1958).

[18] E. Wahlberg, *Ber.*, **65**, 1857 (1932).

[19] R. Ramasseul and A. Rassat, *Bull. soc. chim. France*, 2214 (1963).

[20] W. H. Brown and G. F. Wright, *Can. J. Chem.*, **35**, 236 (1957).

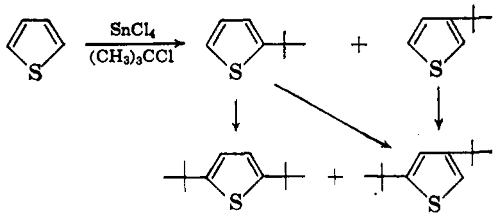
[21] E. Campaigne and W. O. Foye, *J. Org. Chem.*, **17**, 1405 (1952).

analysis and its n.m.r. spectrum (two singlets at τ 8.67 and 8.58 and one at 2.96; area ratio 9:9:1). Decomposition of this saltf urnished gas chromatographically pure 2,4-di-*t*-butylthiophene, b.p. 220.4° (752 mm.), m.p. −1°. Its n.m.r. spectrum is in full accord with its structure showing.singlets at τ 8.75 and 8.65 due to two nonequivalent *t*-butyl groups while two doublets, centered about τ 3.36, have $J_{2,4}$ = 1.50 c.p.s. in excellent agreement with the values given by Gronowitz.[5]

Isomerization.—It was first established that no isomerization of *t*-butyl groups occurred under the influence of stannic chloride, the catalyst used in the alkylation. This realization led immediately to a convenient synthesis of 2,4-di-*t*-butylthiophene. *t*-Butylation of 3-*t*-butylthiophene furnished a di-*t*-butylthiophene identical with the one isolated *via* the mercuric chloride.

The products resulting from the treatment of thiophene with *t*-butyl chloride under these conditions are accounted for in Chart I.

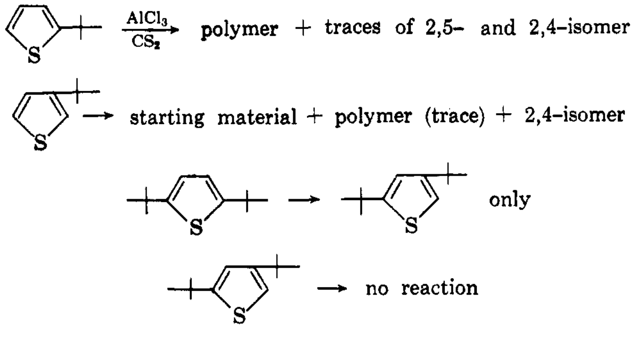
CHART I



Under nonisomerizing conditions, a mixture of 2- and 3-isomers is formed. Further alkylation of the 2-isomer furnishes a mixture of 2,4- and 2,5-dialkylated products, while the 3-isomer furnishes 2,4-di-*t*-butylthiophene only.

Each of the pure mono- and disubstituted isomers was then subjected to rearrangement conditions, *viz.* aluminum chloride in carbon disulfide at room temperature. The results are summarized in Chart II.

CHART II



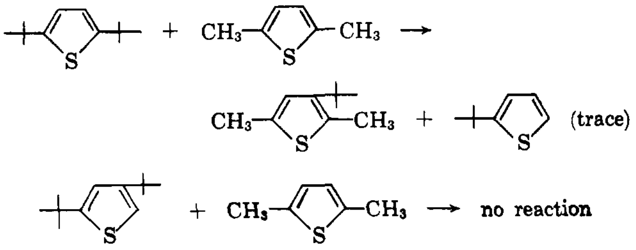
Several conclusions can be drawn from these results. Polymerization of monoalkyl-substituted thiophenes obscures isomerization data. Thus under conditions in which isomerization takes place ($AlCl_3$ in CS_2), polymerization competes if there is an unoccupied α-position. In the case of 3-*t*-butylthiophene, polymerization is nevertheless largely suppressed because the highly reactive 2-position[5] is sterically hindered, while the other α-position (a 5-position) is relatively unreactive.[5] When polymerization is virtually suppressed (by the use of $SnCl_4$ in CS_2), isomerization does not occur.

2,5-Di-*t*-butylthiophene rearranges to 2,4-di-*t*-butylthiophene. This is not unexpected in view of the similarity between *meta* orientation and the 2,4-position in thiophenes.[5] This observation furnishes us with a third and convenient method for the synthesis of 2,4-di-*t*-butylthiophene, starting with the dialkylated mixture of thiophenes.

Transalkylation.—A reasonably good acceptor for transalkylation studies was found to be 2,5-dimethylthiophene. Although no detailed study of its behavior was made, no isomers due to rearrangement of the acceptor itself, using aluminum chloride, were ever found.

The behavior of the *t*-butylthiophenes in the presence of 2,5-dimethylthiophene is shown in Chart III.

CHART III



It was established first that *p*-di-*t*-butylbenzene[22] in the presence of $AlCl_3$ in CS_2 readily alkylated 2,5-dimethylthiophene to form the known[23] 3-*t*-butyl-2,5-dimethylthiophene.

When 2,5-di-*t*-butylthiophene and 2,5-dimethylthiophene were treated with $AlCl_3$ in CS_2, 3-*t*-butyl-2,5-dimethylthiophene was the major product as shown by v.p.c. and the n.m.r. spectrum of the mixture. Owing to the difficulty of detecting 2,4-di-*t*-butylthiophene in the presence of 3-*t*-butyl-2,5-dimethylthiophene, the presence of the former in quantities less than 10% may have gone undetected. 2,4-Di-*t*-butylthiophene itself in the presence of 2,5-dimethylthiophene and $AlCl_3$ in CS_2 showed no tendency to transalkylate. The two independent pieces of evidence we have for the failure of this disproportionation rest on v.p.c. analysis as well as n.m.r. spectra of all of the possible compounds. Once again translkylation to an extent of 10% may have gone undetected (see Chart III).

Experimental

N.m.r. spectra were determined on a Varian A-60 using TMS (τ 10) as internal standard; ultraviolet spectra were determined in 96% alcohol using a Zeiss PMQ II; infrared spectra were determined on a Perkin-Elmer Infracord or 125. All v.p.c. analyses were performed using a 2-m. (0.4-cm. diameter) Apiezon-on-Chromosorb column at 150°. Melting and boiling points are uncorrected. The microanalyses were carried out in this laboratory's analytical department, headed by Mr. W. M. Hazenberg.

2-*t*-Butylthiophene.—To an ice-cooled mixture of 168 g. of thiophene (2.0 moles) and 222 g. of *t*-butyl chloride (2.4 moles) dissolved in 2500 ml. of carbon disulfide, 625 g. of stannic chloride (2.4 moles) was added over a period of 1.75 hr.[9] After hydrolysis of the reaction mixture a fraction of 158 g. (52%) of *t*-butylated thiophenes, b.p. 164–221°, was collected by distillation at atmospheric pressure. Redistillation furnished two

---

[22] R. H. Allen, *J. Am. Chem. Soc.*, **82**, 4856 (1960).

[23] N. Messina and E. V. Brown, *ibid.*, **74**, 920 (1952).

fractions: mono-*t*-butylthiophenes, 122 g., b.p. 164–175°, n^{20}_{D} 1.4986, and di-*t*-butylthiophenes, 29 g., b.p. 210–221°, n^{20}_{D} 1.4936. The lower boiling fraction was fractionated using a 60-plate column. The two best fractions, b.p. 163° (751 mm.), were combined to furnish 10.0 g. of 99% (v.p.c.) pure 2-*t*-butylthiophene, n^{20}_{D} 1.4980. The infrared spectrum was identical with that reported for 2-*t*-butylthiophene by Appleby[8] and Cagniant.[11] Ultraviolet absorption showed $\lambda_{\max}^{96\%\ \text{EtOH}}$ 233 mμ (ϵ 7600); n.m.r. spectrum showed one singlet at τ 8.63 and a multiplet at 3.32–2.96 (area ratio 3:1) (CCl_4 was used in all measurements).

3-*t*-Butylthiophene.—The pot residue from the 60-plate distillation (see above), $n^{20.6}_{\text{D}}$ 1.4989, contained a 1:1 mixture of 2- and 3-*t*-butylthiophene. Using a 30% SE 30 column, 1.5 g. of pure 3-*t*-butylthiophene was obtained by preparative v.p.c. at 145°. The material, n^{20}_{D} 1.5011, was better than 99% pure and its infrared spectrum was identical with that reported.[8] Ultraviolet absorption showed $\lambda_{\max}^{96\%\ \text{EtOH}}$ 234 mμ (ϵ 5500); n.m.r. spectrum showed one singlet at τ 8.70 and a multiplet at 3.15–2.75 (area ratio 3:1).

2,4-Di-*t*-butylthiophene.—Using a 2:1 molar excess of *t*-butyl chloride, 125 g. of thiophene was alkylated for 7 hr. at room temperature, using 530 g. of stannic chloride in 2500 ml. of carbon disulfide. Two distillations furnished 125 g. (43%) of a fraction, b.p. 220–221°, consisting of a mixture of di-*t*-butylthiophenes, free of mono-*t*-butylthiophenes. V.p.c. analysis indicated an isomer ratio of 2,5-di-*t*-butylthiophene to 2,4-di-*t*-butylthiophene of 3:1.

The mixture was chloromercurated, using 230 g. of mercuric chloride and 310 g. of sodium acetate in 6.6 l. of water and 800 ml. of 96% ethanol. The mixture was stirred vigorously for 3 weeks, whereupon 41 g. of light brown powder was removed by filtration. The filtrate furnished 58 g. of 2,5-di-*t*-butylthiophene (purity 95%) upon ether extraction. Recrystallization of the brown solid from ethanol yielded 27 g. of pure 2,4-di-*t*-butyl-5-mercurichlorothiophene, m.p. 117–118°; n.m.r. spectrum showed three singlets at τ 8.67, 8.58, and 2.96 (peak ratio 9:9:1).

Anal. Calcd. for $C_{12}H_{19}ClHgS$ (432.40): C, 33.41; H, 4.44; S, 7.43. Found: C, 33.18; H, 4.52; S, 7.85.

The mercurichloro compound (12 g.) was decomposed by steam distillation from 2 *N* hydrochloric acid furnishing 5.0 g. (90%) of pure (v.p.c.) 2,4-di-*t*-butylthiophene, m.p. −1°, b.p. 220.4° (752 mm.), n^{20}_{D} 1.4916. The infrared spectrum differs from that of the 2,5-isomer and is in agreement with a less symmetrical structure; ultraviolet absorption, $\lambda_{\max}^{96\%\ \text{EtOH}}$ 234 mμ (ϵ 7800); n.m.r. spectrum showed singlets at τ 8.75 and 8.65 and a quadruplet at 3.42, 3.40, 3.35, 3.33 (peak ratio 9:9:2).

Anal. Calcd. for $C_{12}H_{20}S$ (196.35): C, 73.40; H, 10.27; S, 16.33. Found: C, 73.50; H, 10.30; S, 16.30.

2,5-Di-*t*-butylthiophene.—2,2,7,7-Tetramethyloctane-3,6-dione was prepared according to the method of Wahlberg.[18] The ketone, b.p. 110–112° (11 mm.), showed two sharp singlets in the n.m.r. spectrum at τ 8.84 and 7.34 (area ratio 9:2). Five grams of the ketone in 20 ml. of absolute ethanol was treated with hydrogen sulfide and dry hydrogen chloride at 0° as described by Campaigne.[21] The mixture became opaque after 15 min. and an oil separated. V.p.c. analysis showed this oil to be a mixture of 2,5-di-*t*-butylfuran and 2,5-di-*t*-butylthiophene. By continuing the gas stream for 5 hr. adding 2 ml. of water during this period, all of the furan was converted to the thiophene. In this manner 3.9 g. (78%) of v.p.c. pure 2,5-di-*t*-butylthiophene, b.p. 222° (751 mm.), m.p. 22–23°, n^{20}_{D} 1.4930, was obtained; ultraviolet absorption, $\lambda_{\max}^{96\%\ \text{EtOH}}$ 239 mμ (ϵ 9000); n.m.r. spectrum showed two singlets at τ 8.67 and 3.55 (area ratio 9:1).

Anal. Calcd. for $C_{12}H_{20}S$ (196.35): C, 73.40; H, 10.27; S, 16.33. Found: C, 73.55; H, 10.25; C, 16.29.

2,5-Di-*t*-butylfuran could be converted to the corresponding thiophene in 60% yield using the method described above.

2,5-Di-*t*-butylfuran.—When 3.0 g. of 2,2,7,7-tetramethyloctane-3,6-dione[18] was stirred for 24 hr. with 4.0 g. of phosphorus pentoxide at 30°, 2.1 g. (80%) of pure 2,5-di-*t*-butylfuran,[19,20] b.p. 170–171° (772 mm.), n^{20}_{D} 1.4372, was obtained without purification; ultraviolet absorption, $\lambda_{\max}^{n\text{-hexane}}$ 218 mμ (ϵ 10,500); n.m.r. spectrum showed singlets at τ 8.75 and 4.33 (area ratio 9:1).

Anal. Calcd. for $C_{12}H_{20}O$ (180.28): C, 79.93; H, 11.18. Found: C, 80.13; H, 11.14.

***t*-Butylation of 2- and 3-*t*-Butylthiophene.**—3-*t*-Butylthiophene (600 mg., 0.005 mole) and 1.0 g. of *t*-butyl chloride (0.012 mole) dissolved in 10 ml. of carbon disulfide was treated dropwise at room temperature with 3.0 g. of stannic chloride (0.008 mole) in 10 ml. of carbon disulfide. The progress of the reaction was followed by v.p.c. after hydrolysis of a sample. The addition of 20 μl. of water catalyzed the reaction. After 9 days all of the 3-*t*-butylthiophene had been alkylated. V.p.c. showed that 2,4-di-*t*-butylthiophene was the *only* product.

When 2-*t*-butylthiophene was allowed to react in a similar manner, the reaction was complete in 2 days. The products, 2,5-di-*t*-butylthiophene and 2,4-di-*t*-butylthiophene, were present in a ratio of 9:1. This ratio did not change upon stirring for a total of 9 days.

Isomerization and Transalkylation. General.—All experiments were performed using 10% concentrations in carbon disulfide. The molar ratio of reactant to aluminum chloride was 1:1. Room temperature was used throughout unless indicated otherwise. A combination of v.p.c. and n.m.r. spectroscopy was used to analyze the reaction mixtures from a knowledge of the v.p.c. and n.m.r. characteristics of the pure components.

2,4-Di-*t*-butylthiophene with Aluminum Chloride.—Only starting material was found to be present when 2,4-di-*t*-butylthiophene (1.0 g.) was treated with 0.6 g. of aluminum chloride in carbon disulfide for 3 days.

2,5-Di-*t*-butylthiophene with Aluminum Chloride.—When this isomer was treated in a similar manner, 20% of 2,4-di-*t*-butylthiophene was formed after 6 hr. The reaction was complete in 5 days when 95% of the material present was shown to be the 2,4-isomer.

2-*t*-Butylthiophene with Aluminum Chloride.—After 24 hr. of treatment as described above, 15% starting material, traces of both 2,4- and 2,5-isomer, and polymer were detected in the reaction mixture.

3-*t*-Butylthiophene with Aluminum Chloride.—This isomer furnished a mixture consisting of starting material and 2,4-di-*t*-butylthiophene (exclusively) in a 2:3 ratio after 24 hr.

***p*-Di-*t*-butylbenzene and 2,5-Dimethylthiophene with Aluminum Chloride.**—When an equimolar mixture of these two aromatics was treated with aluminum chloride in carbon disulfide, a 20% conversion to 3-*t*-butyl-2,5-dimethylthiophene was obtained in 3.5 hr., together with the equivalent amount of *t*-butylbenzene.

2,5-Di-*t*-butylthiophene and 2,5-Dimethylthiophene with Aluminum Chloride.—A 30% conversion of 3-*t*-butyl-2,5-dimethylthiophene was obtained when the di-*t*-butyl- and dimethylthiophene were allowed to react for 20 hr. A trace of 2-*t*-butylthiophene was shown to be present.

2,4-Di-*t*-butylthiophene and 2,5-Dimethylthiophene with Aluminum Chloride.—After 20 hr. only starting materials could be detected in the reaction mixture.